

LONG-READ SEQUENCING IDENTIFIED NOVEL CITRATE SYNTHASE VARIANT CONTRIBUTING TO METASTATIC PHENOTYPE THROUGH METABOLIC ALTERATIONS IN COLORECTAL CARCINOMA

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Poster

Colorectal

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A novel alternatively spliced isoform of citrate synthase (Δ CS) is overexpressed in colorectal carcinoma and associated with metastasis, recurrence, and worse survival outcomes in stage III and IV patients.

KEY POINTS

- The Δ CS isoform was identified by long-read sequencing in CRC organoids and validated in 97 patient tissue pairs, showing significant overexpression in tumor tissue ($p < 0.001$) with 80.4% of patients demonstrating increased tumor expression.
- High Δ CS expression was significantly associated with recurrence ($p < 0.01$) and lower progression-free survival ($p < 0.01$) and disease-free survival ($p < 0.005$), with particularly worse outcomes in stage III and IV patients (OS and PFS both $p < 0.005$).
- Functional studies showed that Δ CS silencing inhibited cell proliferation and increased apoptosis more profoundly than CS-WT knockdown, while Δ CS overexpression enhanced migration ability in vitro and in vivo.
- The dimerization effect by Δ CS leads to enhanced citrate synthase enzymatic activity, and GC-MS profiling revealed a metabolic shift to amino acid synthesis.
- This material would be most relevant to researchers investigating CRC metastasis mechanisms and therapeutic targets, particularly those focused on metabolic reprogramming in cancer.

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